REMARKS

Claims 1-22 are pending in the present application. The Examiner has acknowledged that claim 1 is allowed. Pursuant to the following remarks, applicants respectfully request reconsideration of the application and allowance of the claims to issue.

Rejection under 35 U.S.C. § 112, first paragraph

The Office Action states that claims 2, 3, 8-16, 21 and 22 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. According to the Office Action, the claims recite portions or parts of either SEQ ID NO: 1 or SEQ ID NO: 2 allegedly not disclosed or exemplified in the specification. The Office Action further alleges that Applicants still fail to teach the parts of nucleotides 1-1134 or parts of nucleotides 28-541 of SEQ ID NO: 2 disclosed in the specification which result in the claimed function.

Applicants reiterate that Applicants have disclosed nucleotides 1-1134 of SEQ ID NO:1 as a sequence which is active as a promoter. Applicants have also disclosed nucleotides 572-1134 of SEQ ID NO: 1 as a part of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter (page 10, lines 10-11 of the specification). Furthermore, it would be clear to one of skill in the art that upon disclosing nucleotides 1-1134 of SEQ ID NO: 1 and parts thereof, Applicants have also disclosed every subsesequence that is a part of nucleotides 1-1134 of SEQ ID NO: 1 and have therefore described the complete structure of each subsequence. For example, it would be clear to one of skill in the art that a part of nucleotides 1-1134 of SEQ ID NO:1 can be nucleotides 1-1133, nucleotides

1-1132, nucleotides 1-1131, nucleotides 2-1134, nucleotides 2-1133, nucleotides 2-1132 etc. because these subsequences are parts of a specifically defined nucleotide sequence. Thus, there is no question as to which nucleotides constitute a subsequence or a part of nucleotides 1-1134 of SEQ ID NO: 1. Furthermore, Applicants have provided a functional limitation for the claimed subsequences. It is clear that the present invention provides a function for nucleotides 1-1134 of SEQ ID NO: 1 as a promoter. Clear guidance for assessing promoter activity of the claimed subsequences or parts of nucleotides 1-1134 of SEQ ID NO: 1 is provided on pages 13-15 as well as throughout the specification where expression of heterologous proteins is described. Furthermore, the characterization of subsequences of a larger promoter sequence is standard and well established practice in the art as evidenced by Li and Schmidt "Characterization and Functional Analysis of the Promoter of RAGE, the Receptor for Advanced Glycation End Products" *J. Biol. Chem.* 272(26) 16498-16506 (1997) and Yamaguchi et al. "Functional Characterization of the Promoter for the Gene Encoding Human Eosinophil Peroxidase" *J. Biol. Chem.* 269(30) 19410-19419 (1994) (Copies attached hereto), which are merely exemplary of the hundreds of references available in the literature describing the characterization of promoter subsequences. For example, Li and Schmidt describe a 1543 base pair 5' flanking region of the human RAGE gene. In order to determine the promoter activity of subsequences of this 1543 base pair sequence, several constructs comprising subsequences of the 1543 base pair promoter fused to luciferase were generated (Li and Schmidt, Fig. 4A). As shown in Figure 4B, the promoter activity for each subsequence could be determined by measuring luciferase activity. It is clear from these results that several subsequences of the 1543 base pair RAGE gene promoter

function as a promoter. Similarly, Yamaguchi et al. describe a human eosinophil peroxidase (EPO) gene promoter of approximately 1500 base pairs. In order to determine the promoter activity of subsequences of this promoter, several constructs comprising subsequences of the 1500 base pair promoter fused to luciferase were generated (Yamaguchi et al., Fig. 5A and 5B). As shown in Figure 5A and 5B, the promoter activity for each subsequence could be determined by measuring luciferase activity. It is clear from these results that several subsequences of the 1500 base pair human EPO promoter function as a promoter. Therefore, given that one of skill in the art can readily obtain subsequences with defined sequences from larger promoter sequences and assess them for promoter activity, there should be no question that every subsequence of nucleotides 1-1134 of SEQ ID NO: 1 can be envisioned by one of skill in the art and assessed for promoter activity. Furthermore, having established that nucleotides 1-1134 of SEQ ID NO: 1 and nucleotides 572-1134 of SEQ ID NO: 1 function as promoters, any subsequence of nucleotides 1-1134 of SEQ ID NO: 1 can be routinely generated and its promoter activity as compared to the promoter activity of nucleotides 1-1134 of SEQ ID NO: 1, can be assessed.

Having established what is set forth in the specification by Applicants and what is considered general knowledge and skill in the art for analyzing promoter sequences, Applicants would like to direct the Examiner's attention to Example 15 on page 56 of the "Revised Interim Written Description Guidelines Training Materials" (publicly available on the Home Page of the USPTO) and referred to herein as the "Guidelines." In Example 15 of the Guidelines, the following claim is set forth:

" An antisense oligonucleotide complementary to a messenger RNA having SEQ ID NO: 1 and encoding human growth hormone, wherein said oligonucleotide inhibits the production of human growth hormone."

According to the Guidelines, the claims in Example 15 are drawn to the genus of antisense molecules that inhibit the production of human growth hormone encoded by SEQ ID NO: 1. There is a single species described with a complete structure, i.e., the full length complement of SEQ ID NO: 1. In addition to the full-length complement, the genus includes fragments of the complement that retain antisense activity. The Guidelines acknowledge that the procedures for making oligonucleotide fragments of the SEQ ID NO: 1 complement are conventional, e.g. any specified fragment can be ordered from a commercial synthesizing service. The procedures for screening for antisense activity are also conventional, and the specification describes an assay needed to do gene walking. The experience accumulated in the art with gene walking is that numerous regions of a target are accessible, that these regions are identified routinely and that antisense oligonucleotides are complementary to these accessible regions. The full-length complement and longer fragments match multiple accessible regions; shorter fragments match fewer accessible regions. The Guidelines also state that "when considering the distinguishing characteristics of the claimed invention, the sequence provided in the specification defines and limits the structure of any effective antisense molecules. The specification also teaches the functional characteristics of the claimed invention as well as a routine art recognized method of making and screening for the claimed invention. According to the Guidelines for Example 15, "[c]onsidering the

specification's disclosure of:

1) the sequence of SEQ ID NO: 1 which defines and limits the structure of any effective antisense molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and
2) the functional characteristics of the claimed invention as well as a routine art-recognized method of screening for antisense molecules which provide further distinguishing characteristics of the claimed invention, along with
3) the general level of knowledge and skill in the art, one skilled in the art would conclude that applicant was in possession of the invention." (Emphasis added)

Therefore, the Guidelines conclude that the claimed invention is adequately described.

The following presents an analysis of the present claims based on the Revised Interim Written Description Guidelines Training Materials and more specifically based on the analysis undertaken in Example 15 of these Guidelines.

Claims 2, 3, 8-16, 21 and 22 of the present invention are drawn to a genus of sequences comprising nucleotides 1-1134 of SEQ ID NO: 1 or a part of the sequence of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter. There are two species described with a complete structure that functions as a promoter, i.e., the sequence of nucleotides 1-1134 of SEQ ID NO: 1 and the sequence of nucleotides 572 - 1134 of SEQ ID NO: 1. In addition to these two species, the genus includes other fragments of the sequence of nucleotides 1-1134 of SEQ ID NO: 1 that retain promoter activity.

As set forth above, guidance for assessing promoter activity is provided in the specification on pages 13-15 as well as throughout the specification where expression of

heterologous proteins is described. Furthermore, as set forth above and exemplified in the attached references (Li and Schmidt; Yamaguchi et l.) the characterization of subsequences of a larger promoter sequence is standard and well established practice in the art. Therefore, there can be no doubt that one of skill in the art would readily be able to assess promoter activity for any subsequence of nucleotides 1-1134 of SEQ ID NO: 1.

When considering the distinguishing characteristics of the claimed invention, the sequence provided in the specification defines and limits the structure of any effective promoter. In essence, by providing nucleotides 1-1134 of SEQ ID NO: 1, there is no question that every single subsequence is derived from a defined and limited structure, i.e. nucleotides 1-1134 of SEQ ID NO: 1. The specification also teaches the functional characteristics of the claimed invention (e.g. promoter activity) as well as a routine art recognized method of making and assessing promoter activity for the sequences utilized in the claimed invention.

Therefore, considering the specification's disclosure of:

1) the sequence of nucleotides 1-1134 of SEQ ID NO: 1 which defines and limits the structure of any effective promoter molecule such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and

2) the functional characteristics of the claimed invention as well as routine methods of assessing promoter activity set forth in the specification and in the art, which provide further distinguishing characteristics of the claimed invention, along with

3) the general level of knowledge and skill in the art, one skilled in the art

would conclude that Applicants were in possession of the invention.

Therefore, the Office should conclude that the claimed invention is adequately described.

The same analysis applies to the terminator sequences utilized in the claimed invention. Claims 2, 3, 8-16, 21 and 22 are drawn to a genus of sequences comprising nucleotides SEQ ID NO: 2 or a part of the sequence of SEQ ID NO: 2 which functions as a terminator. There are two species described with a complete structure, i.e., SEQ ID NO: 2 and the sequence of nucleotides 28-542 of SEQ ID NO: 2. In addition to these two species, the genus includes other fragments of SEQ ID NO: 2 that function as a terminator.

Guidance for assessing terminator activity is provided in the specification on pages 13-15 as well as throughout the specification where expression of heterologous proteins is described. One of skill in the art would clearly be able to obtain any subsequence of SEQ ID NO: 2 and determine if this subsequence functions as a terminator by utilizing the subsequence of SEQ ID NO: 2 in an expression system, as described by Applicants on pages 13-15. Thus, it is routine to determine whether or not a sequence serves as a terminator for a protein.

When considering the distinguishing characteristics of the claimed invention, the sequence provided in the specification defines and limits the structure of any effective terminator. In essence, by providing the nucleotides of SEQ ID NO: 2, there is no question that every single subsequence that functions as a terminator is derived from a defined and limited structure, i.e. SEQ ID NO: 2. The specification also teaches the functional characteristics of the claimed invention (e.g. terminator activity) as well as a

routine art recognized method of making and assessing terminator activity for the sequences utilized in the claimed invention.

Therefore, considering the specification's disclosure of:

1) the sequence of SEQ ID NO: 2 which defines and limits the structure of any effective terminator molecule such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and
2) the functional characteristics of the claimed invention as well as routine methods of assessing terminator activity set forth in the specification and in the art, which provide further distinguishing characteristics of the claimed invention, along with
3) the general level of knowledge and skill in the art, one skilled in the art would conclude that Applicants were in possession of the invention.

Therefore, the Office should once again conclude that the claimed invention is adequately described.

Thus, with regard to the Examiner's statement that Applicant has not specifically defined any of the parts or portions of the sequences claimed that fall within the broad genus claimed, Applicants respectfully point out that if the Office deems that given a sequence of defined and limited structure, one of skill in the art could immediately envisage any antisense molecule that is complementary to that sequence, one of skill in the art could immediately envisage any subsequence of nucleotides 1-1134 of SEQ ID NO:1 and any subsequence of SEQ ID NO: 2. Furthermore, these subsequences with defined structures possess a functional characteristic which further distinguishes the characteristics of the claimed invention. Therefore, contrary to the Examiner's assertion,

Applicants have specifically defined all of the parts or portions of 1-1134 of SEQ ID NO:1 that function as a promoter and all of the parts or portions of SEQ ID NO: 2 that function as a terminator.

Furthermore, with regard to the Examiner's statement that Applicants allegedly fail to describe any structural characteristics commonly possessed by members of the genus such that one of skill in the art would recognize that Applicants were in possession of the full breadth of the invention claimed and that the functional limitation allegedly does not adequately described the claimed genus, Applicants respectfully point out that Applicants are claiming members of the genus encompassing subsequences of 1-1134 of SEQ ID NO: 1 that also possess promoter activity. Similarly, Applicants are claiming all of the members of the genus encompassing subsequences of SEQ ID NO: 2 that also possess terminator activity. Thus, it is the combination of a sequence derived from the the sequence of nucleotides 1-1134 of SEQ ID NO: 1 which defines and limits the structure of any effective promoter such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and the functional characteristics of the claimed invention as well as routine methods of assessing promoter activity that would lead one skilled in the art to conclude that Applicants were in possession of the invention. Similarly, it is the combination of a sequence derived from SEQ ID NO: 2 which defines and limits the structure of any effective terminator such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and the functional characteristics of the claimed invention as well as routine methods of assessing terminator activity that would lead one skilled in the art to conclude that Applicants were in possession of the claimed invention. Thus, it is clear

that Applicants are claiming a genus of defined and limited structures that have a functional activity and not merely utilizing a functional limitation to describe the claimed genus. Therefore, for all of the reasons set forth above, Applicants believe that claims 2, 3, 8-16, 21 and 22 are adequately described such that one of skill in the art would know that Applicants were in possession of the claimed invention. Thus, Applicants believe this rejection has been overcome and respectfully request its withdrawal.

Rejection under 35 U.S.C. § 112, first paragraph

The Office Action states that claims 4-7 and 17-20 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. According to the Office Action, where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. § 112. Further stated in the Office Action is that Applicants claim various plasmid constructs in the instant claims and that in order to enable the claimed plasmids, Applicant must make a biological deposit of each of them in addition to making assurances of availability.

As set forth in the specification on page 5, lines 24-27, "[t]he plasmids are contained in the micro-organisms DSM 12919, DSM 12920, DSM 12921 or DSM 12922* and are deposited therewith [*Deposited on July 13, 1999 at DSMZ, Mascheroder Weg 1b, 38124 Braunschweig]." Thus, Applicants have already deposited the claimed plasmids with the DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) (Mascheroder Weg 1b, D-38124 Braunchweig, Germany),

an International Depositary Authority recognized under the Budapest Treaty. For the convenience of the Office, attached hereto are the deposit receipts for DSM 12919, DSM 12920, DSM 12921 and DSM 12922 which were deposited with the DSMZ on July 13, 1999 under the Budapest Treaty. Thus, the same plasmids and microorganisms that were described in the specification on page 5, lines 24-27 are the same plasmids and microorganisms that were deposited with the DSMZ on July 13, 1999 and satisfy the availability requirements of the Budapest Treaty. Furthermore, all restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent. Therefore, Applicants believe this rejection has been overcome and respectfully request its withdrawal.

A Credit Card Payment Form PTO-2038 authorization payment in the amount of $1020 (Extension of Time fee) and a Request for Extension of Time are included herewith. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

In view of the above amendments and remarks, reconsideration and allowance of the pending claims is believed to be warranted, and such action is respectfully requested. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issuance.

Respectfully submitted,

NEEDLE & ROSENBERG, P.D.

Lizette M. Fernandez, Ph.D.
Reg. No. 46,694

NEEDLE & ROSENBERG, P.C.
Customer Number 23859
(678) 420-9300
(678) 420-9301 (fax)

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date indicated below.

Lizette M. Fernandez — Date: 5/31/05